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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/616,283	07/14/2000	Timothy T. Goodnow	109. 111. 114	6499

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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	25

DATE MAILED: 09/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/616,283	GOODNOW, TIMOTHY T.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this c mmunicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,14-18 and 23-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 14-18 and 23-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. The amendment filed August 13, 2003 has been entered. Claim 35 has been newly added. Claims 19-22 and 24 have been cancelled. Claims 1-8, 14-18, 23 and 25-35 are under consideration.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments:

a) The rejection of claims 1, 3-6, 14 and 16 under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461, 462) in view of McLaughlin and Tadler et al;

b) The rejection of claims 2 and 15 under 35 U.S.C. 103(a) as being unpatentable over Chan, McLaughlin and Tadler et al., as applied to claims 1 and 14 above, and further in view of Chang et al., (US Patent 5,200,323);

c) The rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461,462) in view of Tadler et al., (1989); and

d) The rejection of claims 8 and 18 under 35 U.S.C. 103(a) as being unpatentable over Chan (EP 461,462) in view of McLaughlin (US Patent 4,683,196).

New Grounds For Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-8,14-18, 23 and 25-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a pan-generic monoclonal antibody that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A clone 26-5, a detection step, wherein binding indicates the presence of a clinically relevant amount of bacteria in the donor blood or blood product, does not reasonably provide enablement for a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a set of binding agents, wherein the set of pan-generic binding agents specifically bind to a gram-negative/positive bacterial antigen and determining the binding. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

The claims are drawn to a method for screening for the presence of a clinically relevant amount of bacteria in a donor blood or blood product from a donor mammal for transfer to a recipient mammal comprising contacting a sample of the donor blood or blood product with a set of pan-generic binding agents, wherein the set of pan-generic

binding agents specifically bind to a gram-negative/positive antigen and determining the binding of said agents for the presence or absence of the bacterial antigen.

The specification only teaches pan-generic monoclonal antibodies that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A clone 26-5. The specification fails to teach examples of other pan-generic binding agents that specifically bind to a gram-negative/positive antigen and determining the binding of said agents for the presence or absence of the bacterial antigen. The specification appears to make the conclusion that any binding agent can be pan-generic and adequate to the determine binding and/or presence of gram positive and negative bacterial antigens. Therefore, the claims are only enabled for the use of the pan-generic monoclonal antibody that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid, clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A, clone 26-5. Example 9 in the specification is the only teaching pan-generic binding agents, moreover example 9 is only drawn to the specific pan-generic monoclonal antibodies. There is no teaching of other binding agents being pan-generic. Particularly, claims 23 and 25 recite binding agents such as antibiotics, MBP, toll-like receptor-2 and histatins, however these agents do not appear to have the pan-generic capabilities. Therefore, these claims are not enabled since there is no teaching that these agents are pan-generic.

Without the specific pan-generic monoclonal antibody that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid, clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A, clone 26-5 to indicate binding of the complex, one of ordinary skill in the art could not determine whether the other binding agents are capable of binding multiple species of bacteria in order to meet the limitations of the instant claims. In view of specification that teaches the use of pan-generic monoclonal antibodies that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid, clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A, clone 26-5, undue experimentation would be required to locate de novo other pan-generic binding agents that would determine binding and detection of bacterial antigens. There is no guidance to enable one of ordinary skill in the art how to make, without undue experimentation, to determine the presence or absence of the bacteria wherein the set of binding agents are pan-generic. Given the lack of guidance contained in the specification for detecting bacterial antigens without a pan-generic monoclonal antibody that specifically binds to the gram-positive bacterial antigen Lipoteichoic acid, clone 96-110 and/or a pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A, clone 26-5, one of skill in the art could not make or use the broad claimed invention without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 1, 3-6, 14-17,23, 25, and 27-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlin, Erich et al., Tadler et al., and Fischer et al.

McLaughlin teaches methods and materials for the identification of lipopolysaccharide (LPS) producing microorganisms. The structure of LPS has been described in studies of gram-negative bacteria, wherein the middle region is a conserved region (col. 1 lines 30-35). The shared antigen is often a component of the LPS, thereby allowing detection of gram-negative microorganisms such as *Neisseria, Brucella, Escherichia, Salmonella* and the like (col. 2 lines 60-66 and col. 5 lines 10-22). One of the antigenic determinant sites includes the glyocolipid antigen associated with endotoxins or endotoxin-like molecules produced by gram-negative microorganisms (col. 4 lines 20-25). The immunological detection of an entire class of microorganism within a sample is taught (col. 2 lines 45-47). A clinical sample may be defined as body fluids or secretions such as blood, serum, saliva, stool, topical washing of skin or genitals, tissue samples or homogenates thereof (col. 5 lines 65-68). The antibodies can be used in any well-known immunological detection system, such as ELISA, or precipitation or agglutination assays (col. 5 lines 36-54). The authors teach several antibodies to lipid A and endotoxin glycolipids (Table 1). For instance, a clinical sample

contains both *Chlamydia* and *Neisseria*; both organisms are detected by the capture antibody attached to the solid support (col. 6 lines 30-34). Once bound, the addition of two additional types of detectably labeled antibodies would permit simultaneous detection (col. 6 lines 34-36). Other variations employing colorimetric blending of two separate reaction products or the use of a radiometric/photo spectrometric combination is also possible (col. 6 lines 46-48). Example 4 teaches a solid phase immunometric assay. Thus by using a broad spectrum antibody, it is possible to perform a single test for large number of LPS producing organisms by merely reacting the antibody with the clinical sample (col. 5 lines 29-34). However McLaughlin does not teach a the pan-generic monoclonal antibody that specifically binds to the gram-negative bacterial antigen Lipid A clone 26-5.

Erich et al., teach binding characteristics and cross-reactivity of three different anti-lipid A monoclonal antibodies. Antibodies against lipid A are of interest because this structure is conserved among different strains and types of gram-negative bacteria (page 4057). The antibodies bind lipid A, derivatives of Lipid A in solid phase ELISA assays and fluid phase assays (abstract). Cross reactivity with heterologous antigens was investigated in ELISA assays to detect gram-negative bacteria (abstract). Monoclonal 26-5 (IgG2b) showed extensive cross-reactivity with heat-killed as well as live gram-negative bacteria, see tables IV, and VI.

Tadler et al., teach rapid recovery and identification of bacteria in blood that is important in patient management to prevent bacteremia that can present life-threatening situations for several patient populations (page 21). Tadler et al., teach sandwich

immunoassay for the detection of lipoteichoic acid, (LTA) which is a major cell wall constituent of gram-positive bacteria from whole blood (abstract). Monoclonal antibodies to LTA were produced and many reacted exclusively with gram-positive bacteria (abstract). Nine monoclonal antibodies were selected that demonstrated reactivity to gram-positive bacteria but did not cross-react with the panel of gram-negative bacteria (page 22). Table 1 shows that characterization of anti-LTA monoclonal antibodies and its cross-reactivity with gram-positive bacteria. Further development of this assay may lead to rapid detection of LTA from other body fluids (abstract), however this assay is clearly useful in a clinical setting (page 24). Thus Tadler et al., teach contacting a sample of blood with a set of binding agents; wherein specific binding occurs; and binding indicates the presence or absence of a clinically relevant amount of gram-positive bacteria in the blood sample and the identification of blood determined to have an absence of a clinically relevant amount of gram-positive bacteria. However Tadler et al., does not teach the use of monoclonal antibody 96-110.

Fischer et al., teach monoclonal antibodies that bind to lipoteichoic acid of gram-positive bacteria (page 5). The antibodies also bind to whole gram-positive bacteria (page 5). The antibodies are broadly reactive with several gram-positive species and can be used in ELISA assays (page 9). One particular antibody, designated 96-110 exhibited strong IgG reactions (page 13). The antibody can be used in a wide variety of binding assays such as ELISA, radioimmunoassays, fluorescent binding assays, or any other suitable binding assay (page 24). The monoclonal antibody displayed reactivity

with several species of gram-positive *Staphylococcus* bacteria (page 27). Table 5 shows that the monoclonal antibody detects gram-positive bacteria in whole cell ELISA.

It should also be noted, the recitation a method of screening of blood from a donor mammal for transfer to a recipient mammal, as recited in the claims has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). It is noted that the art teaches detection of bacterial antigens in blood or blood product samples, the prior art recites the same purpose as the instant claims.

Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference or additionally positively recited method steps between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Wherein the intended use is "useful for transfer to the recipient mammal". If the prior art method is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. There is no positively recited method step requiring the samples be transferred to a recipient mammal. Thus, the use of the sample is not considered as a limitation. Therefore, the prior art method is capable of performing the intended use, thus it meets the claim.

Therefore, it would have been prima facie obvious to modify the analyte detection immunoassay that incorporates a set of binding agents as taught by McLaughlin and Tadler et al., since McLaughlin and Tadler et al., teach antibodies which specifically bind to gram-negative or gram-positive bacteria in order to determine their presence and/or absence wherein the assay is modified to include the pan-generic monoclonal antibodies as taught by Erich et al., and Fischer et al. Thus, one would have a reasonable expectation of success in utilizing a set of binding agents that bind to gram-negative and positive bacteria detection assays in a known analyte detection assays to test samples of blood, since pan-generic antibodies are known for their ability to detect several species and types of bacteria. Moreover McLaughlin and Tadler et al, teach samples suitable for practice of the method of detection to include whole blood, serum, and tissue and/or fluids, while Erich et al., and Fisher et al., teach pan-generic antibodies useable in immunoassays.

5. Claims 2 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlin, Erich et al., Tadler et al., and Fisher et al., as applied to claims 1 and 14 above, and further in view of Chang et al., (US Patent 5,200,323). McLaughlin, Erich et al., Tadler et al., and Fisher et al., have all been discussed above, however none teach that in the absence of a clinically relevant amount of bacteria is transferred to a recipient mammal.

Chang et al., teach transfusion of blood from donor to recipient is a form of transplantation (col. 1 lines 8-10). However, bacterial infection, despite careful preparation from blood draws may contain a few bacteria (col. 2 lines 31-33). Thus it would be highly desirable to provide in vitro screening test that would be based on human blood or plasma to determine the safety of modified hemoglobin for humans prior to clinical use; to provide a bridge between animal testing and human clinical trials and to rule out potential problems before starting the clinical trials (col. 4 lines 10-30).

Therefore, it would have been prima facie obvious to modify the method of screening by using blood or blood product determined to have an absence of clinically relevant amount of bacteria as taught by as taught by McLaughlin, Erich et al., Tadler et al., and Fisher et al., since Chang et al., teach it is beneficial to screen blood to prevent contamination. Thus, one would have a reasonable expectation of success in utilizing blood screened with in vitro screening assays to determine the safety of the blood prior to clinical use. Moreover McLaughlin, Erich et al., Tadler et al., and Fisher et al., all teach in vitro screening assays capable of determining the presence or absence of a bacterial antigen.

6. Claims 7 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tadler et al., (1989) and Fisher et al. The claims are drawn to methods for screening for the presence of pan-generic binding agents that bind gram-positive bacterial antigens. Tadler and Fischer et al., have been discussed above, along with the preamble language and intended use recitation. However Tadler et al., do not teach a pan-generic gram-positive binding agents that specifically bind gram-positive bacteria.

Therefore, it would have been prima facie obvious to modify the multiple analyte detection immunoassay using a set of binding agents wherein the sample is blood or a blood product as taught by Tadler et al., since Tadler et al., teach antibodies which specifically bind to gram-negative bacteria in order to determine their presence and/or absence while Fischer et al., teach using well-known pan-generic monoclonal binding that bind Lipid A of gram-negative bacteria. Thus, one would have a reasonable expectation of success in utilizing a pan-generic binding agents that bind to gram-negative assays in a known multiple analyte simultaneous detection assays to test samples of blood since the prior art teach such steps are well-known. Moreover Tadler et al., teach samples suitable for practice of the method of detection to include whole blood, serum, and tissue samples, with the same detection steps as recited by the instant claims.

7. Claims 8 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlin in view of Erich et al. The claims are drawn to methods for screening for the presence of pan-generic binding agents that bind gram-negative bacterial antigens.

McLaughlin and Erich et al., have been discussed above, along with the preamble language and intended use recitation. However McLaughlin did not teach a pan-generic gram-positive binding agents that specifically bind gram-positive bacteria.

Therefore, it would have been prima facie obvious to modify the multiple analyte detection immunoassay using a set of binding agents wherein the sample is blood or a blood product as taught by McLaughlin since McLaughlin teach antibodies which specifically bind to gram-negative bacteria in order to determine their presence and/or absence while Erich et al., teach using well-known pan-generic monoclonal binding that bind Lipid A of gram-negative bacteria. Thus, one would have a reasonable expectation of success in utilizing a pan-generic binding agents that bind to gram-negative assays in a known multiple analyte simultaneous detection assays to test samples of blood since the prior art teach such steps are well-known. Moreover McLaughlin teaches samples suitable for practice of the method of detection to include whole blood, serum, and tissue samples, with the same detection steps as recited by the instant claims

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers

for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
September 24, 2003

LYNETTE R. F. SMITH
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